Remarks

Claims 1, 4-5, 9, 15, and 36 are amended herein; and claims 2-3, 8, 13-14, 18-32, 34-35, 38-39, and 42-45 are canceled. As a result, claims 1, 4-7, 9-12, 15-17, 33, 36-37, 40-41, and 46-47 are pending in this application. Claims 10-12, 16-17, 40-41, and 46-47 are withdrawn from consideration.

The amendments to the claims are supported throughout the specification. Amended claim 1 is supported, e.g., by originally filed claims 1, 3, 8, and 9. Amended claims 4, 5, 9, 15, are supported, e.g., by the corresponding originally filed claims. Amended claims 36 is supported, e.g., at paragraph 28 on page 9 of the specification.

Claim Objections

Claims 8 and 9 were objected to for reciting antigens drawn to non-elected subject matter. Claim 8 is canceled. Claim 9 depends from claim 1. Claim 1 has been amended to recite the elected subject matter – a composition comprising at least two antigens wherein one of the two antigens is a bacterial antigen and the other is a candida antigen. Claim 9 depends from claim 1 and thus is drawn to the elected subject matter.

The Rejection of the Claims Under 35 U.S.C. § 112, Second Paragraph

Claims 34-35 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 34-35 have been canceled.

The Rejection of the Claims Under 35 U.S.C. § 112, First Paragraph

Claims 1-7, 13-15, and 33-39 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This rejection is respectfully traversed insofar as it may apply to the amended claims.

The Examiner has stated that the application meets the written description requirement for a pharmaceutical composition comprising a bacterial antigen and a candida antigen where each antigen is capable of inducing a cutaneous DTH response. The claims have been amended accordingly. Thus, Applicant believes that the present claims satisfy the written description requirement of 35 U.S.C. § 112, paragraph 2.

Claims 1-9, 13-15, and 33-39 were rejected under 35 U.S.C. § 112, first paragraph, because, the Examiner stated, the specification, while being enabling for a pharmaceutical composition for treating a benign epithelial tumor, does not reasonably provide enablement for a pharmaceutical composition for treating any type of epithelial tumor including cervical carcinomas or melanomas. This rejection is respectfully traversed insofar as it may apply to the amended claims.

The claims have been amended to recite a pharmaceutical composition wherein the composition is capable of treating a benign epithelial tumor caused by a papilloma virus in a mammalian subject. Recitation of a cervical carcinoma and a melanoma in claim 5 has been deleted. Applicant believes that the amendments to the claims obviate the basis for the enablement rejection.

In view of the amendments and remarks herein, withdrawal of the rejections of the claims under 35 U.S.C. § 112, first paragraph, is respectfully requested.

The Rejection of the Claims Under 35 U.S.C. § 102(e)

Claims 1-9, 13-14, 33-36, and 38 were rejected under 35 U.S.C. § 102(e) as anticipated by Clements (U.S. Patent No. 6,033,673). This rejection is respectfully traversed.

Clements discloses a novel mutant of *E. coli* heat labile enterotoxin modified by two amino acid substitutions and designated LT(R192G/L211A) (abstract). It discloses that the mutant enterotoxin can be administered in conjunction with any biologically relevant antigen or vaccine, such that an increased immune response to the antigen or vaccine is achieved (col. 9, lines 36-41). It discloses that the mutant enterotoxin and antigen can be administered simultaneously in a pharmaceutical composition (col. 9, lines 43-45). It discloses that useful antigens include antigens from pathogenic fungi,

including *Candida albicans* (col. 10, lines 27-29). It discloses that the mutant enterotoxin promotes the production of serum and/or mucosal antibodies as well as cell-mediated immune responses against antigens that are simultaneously administered with the mutant enterotoxin (col. 9, lines 6-10).

The pending claims recite that each of the two antigens in the pharmaceutical composition – the bacterial antigen and the antigen selected from the group consisting of candida, trichophyton, and mumps antigens – induces or is capable of inducing a cutaneous delayed type hypersensitivity reaction. Clements does not disclose that LT(R192G/L211A) on its own induces or is capable of inducing any cell-mediated response, or specifically a cutaneous delayed type hypersensitivity response, as recited in the present claims. Clements does not even disclose that LT(R192G/L211A) is an antigen itself. Clements only discloses that administered with an antigen LT(R192G/L211A) may promote a cell-mediated immune response against the antigen (col. 9, lines 6-10; col. 13, line 62-col. 14, line 9).

A reference anticipates a claim under 35 U.S.C. § 102, "only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." M.P.E.P. §2131; *Verdegaal Bros. v. Union Oil Co. of California* 814 F.2d 628,631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Clements does not disclose that LT(R192G/L211A) is an antigen at all, or that it induces or is capable of inducing on its own a cutaneous delayed type hypersensitivity response. Accordingly, Clements does not disclose all the elements of any of claims 1, 4-7, 9, 15, 33, 36-37, or 42-43 and does not anticipate any of the claims.

Claims 1-9, 13-14, 33-36, and 38 were rejected under 35 U.S.C. § 102(e) as anticipated by Bostwick (U.S. Published Patent Application 2002/0009429 A1). This rejection is respectfully traversed.

Bostwick was filed on January 29, 1999, less than one year before the filing date of the parent application of the present divisional patent application. The priority date of the present application is June 25, 1999.

The attached Rule 131 Declaration of one of the inventors, Thomas Dag Horn, establishes conception of the presently claimed invention before the filing date of Bostwick and diligence until the filing of the priority patent application. Dr. Horn cites

in his declaration an approval letter dated before the filing date of Bostwick approving his plans to use mumps and candida skin test antigens to treat humans afflicted with verruca vulgaris (common warts) (paragraph 4). Dr. Horn also declares that at that time he also believed that any antigen that induced a cutaneous delayed-type hypersensitivity response, including bacterial antigens, would successfully treat warts and other benign epithelial tumors. Dr. Horn further declares that before the filing date of Bostwick, Dr. Horn planned to combine two or more antigens in a single composition to be administered for treatment of warts and other epithelial tumors. He states that the compositions with two or more antigens that he had conceived at that time included compositions containing candida and bacterial antigens (paragraph 4). These facts establish conception of the presently claimed invention before the filing date of Bostwick.

Dr. Horn declares further that after receiving the approval letter from Dr. Faas cited in his declaration, he proceeded to conduct the studies in humans that it refers to, successfully treating Verruca vulgaris in humans with the antigenic compositions. He declares that after accumulating some data on treatment of humans, the data and a description of the invention were submitted to a patent attorney for filing of a patent application, which was filed on June 25, 1999. These facts establish diligence from prior to the filing date of Bostwick until filing of the parent to the present patent application.

The Rule 131 Declaration of Dr. Horn establishes conception of the presently claimed invention before the filing date of Bostwick and diligence from before the filing date of Bostwick until filing of the priority patent application on June 25, 1999. This removes Bostwick as prior art.

Accordingly, withdrawal of the rejection of claims 1-9, 13-14, 33-36, and 38 under 35 U.S.C. § 102(e) as anticipated by Bostwick (U.S. Published Patent Application 2002/0009429 A1) is respectfully requested.

In view of the amendments and remarks herein, withdrawal of the rejections of the claims under 35 U.S.C. § 102(e) as anticipated by Clements (U.S. Patent No. 6,033,673) or Bostwick (U.S. Patent Application Publication No. 2002/0009429) is respectfully requested.

The Rejection of the Claims Under 35 U.S.C. § 103(a)

Claims 1-9, 13-15, and 33-39 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Bostwick (US 2002/0009429) or Clements (U.S. Patent No. 6,033,673) in view of the CANDIN package insert text. This rejection is respectfully traversed.

Bostwick is removed as prior art by the Rule 131 Declaration of Dr. Horn, as discussed above.

Three criteria must be met in order to establish a *prima facie* case of obviousness. First, the prior art reference (or references when combined) must teach or suggest all the claim limitations. Second, there must be some suggestion or motivation in the references or in the knowledge generally available to one of ordinary skill in the art to modify the reference or combine reference teachings to arrive at the claimed invention. Third, there must be a reasonable expectation of success. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. M.P.E.P. § 2142.

The present claims recite a pharmaceutical composition comprising at least two antigens, wherein (1) each of the antigens induces or is capable of inducing a cutaneous delayed-type hypersensitivity response in a mammalian subject; (2) the composition is capable of treating a benign epithelial tumor caused by a papilloma virus in a mammalian subject; and (3) one of the two antigens is a bacterial antigen and the other is a candida antigen.

Clements discloses a novel mutant of *E. coli* heat labile enterotoxin modified by two amino acid substitutions and designated LT(R192G/L211A) (abstract). It discloses that the mutant enterotoxin can be administered in conjunction with any biologically relevant antigen or vaccine, such that an increased immune response to the antigen or vaccine is achieved (col. 9, lines 36-41). It discloses that the mutant enterotoxin and antigen can be administered simultaneously in a pharmaceutical composition (col. 9, lines 43-45). It discloses that useful antigens include antigens from pathogenic fungi, including *Candida albicans* (col. 10, lines 27-29). It discloses that the mutant enterotoxin promotes the production of serum and/or mucosal antibodies as well as cell-mediated immune responses against antigens that are simultaneously administered with the mutant enterotoxin (col. 9, lines 6-10).

Clements does not disclose or suggest that LT(R192G/L211A) on its own induces or is capable of inducing any cell-mediated response, or specifically a cutaneous delayed type hypersensitivity response, as recited in the present claims. Clements does not even disclose that LT(R192G/L211A) is an antigen itself. Clements only discloses that administered with an antigen LT(R192G/L211A) may promote a cell-mediated immune response against the antigen (col. 9, lines 6-10; col. 13, line 62-col. 14, line 9).

Clements also does not disclose or suggest that a composition containing LT(R192G/L211A) and a candida antigen, or any other composition, would be capable of treating a benign epithelial tumor caused by a papilloma virus.

The CANDIN package insert does nothing to remedy these deficiencies.

Clements does not disclose or suggest a composition containing two antigens where each antigen induces or is capable of inducing a cutaneous delayed-type hypersensitivity response in a mammalian subject. Clements also does not disclose or suggest that any composition is capable of treating a benign epithelial tumor in a mammal. Thus, Clements does not teach or suggest all the claim elements.

Clements also does not provide any suggestion or motivation to modify its teachings to arrive at a composition containing at least two antigens that induce or are capable of inducing a delayed-type hypersensitivity reaction in a mammalian subject, wherein the composition is capable of treating a benign epithelial tumor caused by a papilloma virus in a mammalian subject, and wherein one of the two antigens is a bacterial antigen and the other is a candida antigen.

The CANDIN package insert does nothing to remedy these deficiencies of Clements. Accordingly, the cited references fail to satisfy at least two of the three requirements for a *prima facie* case of obviousness. Thus, it is respectfully requested that the Examiner withdraw the rejection of claims 1-9, 13-15, and 33-39 under 35 U.S.C. § 103(a) over Bostwick (US 2002/0009429) or Clements (U.S. Patent No. 6,033,673) in view of the CANDIN package insert text.

Conclusion

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (651-207-8270) to facilitate prosecution of this application.

Respectfully submitted,

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Date Nov. 16, 2004 By: Hugh McTavish

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient first class postage, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 16 day of November, 2004.

Hugh McTavish

Hugh McTavish